

Prior to examination, please amend the above-identified application as follows:

In the Claims:

Please cancel Claim 19 without prejudice or disclaimer as drawn to a non-elected invention.

REMARKS

Claims 1 - 17 are pending. Claim 19 has been canceled without prejudice or disclaimer as it is directed to a non-elected invention. An Appendix of Pending Claims is attached for the Examiner's convenience.

Applicants submit that inventorship has not been changed by the cancellation of Claim 19.

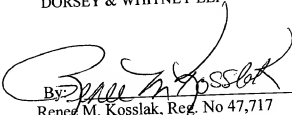
Attached hereto is a marked-up version of the changes made to the claims by this Amendment. The attached page is captioned "Version with Markings to Show Changes Made".

The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues may be resolved in that manner.

Respectfully submitted,

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Version with Markings to Show Changes Made

Claim 19 has been cancelled.

Appendix of Pending Claims

1. A method for modulating the immunogenicity of a target protein, said method comprising:
 - a) inputting a protein backbone structure with variable residue positions of a target protein into a computer;
 - b) computationally generating a set of primary variant amino acid sequences; and,
 - c) applying a computational immunogenicity filter against said set to identify at least one candidate variant protein.
2. A method according to claim 1 further comprising testing said candidate variant protein to determine if said immunogenicity is altered relative to said target protein.
3. A method according to claim 1 further comprising classifying each variable residue position as either a core, surface or boundary residue.
4. A method according to claim 1 wherein said computationally generating step comprises a DEE computation.
5. A method according to claim 4 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.
6. A method according to claim 1 wherein said set of primary variant amino acid sequences are optimized for at least one scoring function.
7. A method according to claim 6 wherein said set of primary variant amino sequences optimized for at least one scoring function comprises the globally optimal protein sequence.
8. (Amended) A method according to claim 6 wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic salvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

9. A method according to claim 1 wherein said computationally generating step includes the use of a Monte Carlo search.

10. A method according to claim 1 wherein said target protein is from a non human species and said candidate variant protein exhibits reduced immunogenicity in humans.

11. A method according to claim 1 wherein the immunogenicity of said candidate variant protein is reduced relative to said target protein.

12. A method according to claim 1 wherein said candidate variant protein is non-immunogenic.

13. A method according to claim 11 or 12 wherein said candidate variant protein is more stable than said target protein.

14. A method according to claim 1 wherein said modulating the immunogenicity of said target protein comprises modifying the amino acid sequence that binds to an MHC molecule.

15. A method according to claim 14 wherein said MHC molecule belongs to MHC class I.

16. A method according to claim 14 wherein said MHC molecule belongs to MHC class II.

17. A method according to claim 1 wherein said modulating the immunogenicity of said target protein comprises modifying an amino acid sequence encoding a T cell epitope.